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## DIAZINON

### GENERAL

Diazinon (o-o-diethyl o-(2-isopropyl-4-methyl-6-pyrimidinyl)-phosphorothioate) is a wide-spectrum organophosphorus insecticide. It has the empirical formula  $C_{12}H_{21}N_2O_3PS$  and a molecular weight of 304.36. The pure material is a colorless liquid with a faint ester-like odor. The boiling point is 83 to 84°C. The density at 25°C is 1.116 to 1.118. The vapor pressure is  $4.1 \times 10^{-4}$  mm Hg at 20°C and  $1.1 \times 10^{-3}$  mm Hg at 40°C. The refractive index is 1.4978 to 1.4981. It is relatively unstable in acid in contrast to many organophosphates. The half-life at a pH of 3.14 is 0.5 day and at a pH of 10.9 is 6 days compared with 185 days at a pH of 7.4. Diazinon decomposes above 120°C and is susceptible to oxidation. The solubility of diazinon in water at 20°C is 40 parts per million (ppm). It is miscible with alcohol, ether, petroleum ether, cyclohexane, benzene, and similar hydrocarbons. Diazinon first was introduced in 1952, and its insecticidal properties were described in 1953. The common name diazinon is in general use and other trade names include Basudin, Diuzitol, Dipofene, Neocidol, Nucidol, and Spectricide. Code designations include G-24480 and OMS-469. The CAS registry number is 333-41-5. Ciba-Geigy Corporation is the major producer of technical diazinon.

### USES

Diazinon is used in the United States for control of soil insects, such as cutworms, wireworms, and maggots. It is also used against many pests of fruits, vegetables, tobacco, forage, field crops, range, pasture, grasslands, and ornamentals. It is used extensively in controlling cockroaches and many other household insects; grubs and nematodes in turf; seed treatment; and fly control. Foreign uses include control of stemborers and leafhoppers in rice, ectoparasites, e.g., mange (on sheep, cattle, and swine), or blow fly (on sheep).

### HEALTH EFFECTS

Diazinon can affect the body if it is inhaled, comes in contact with the eyes or skin, or is swallowed. It may enter the body through the skin.

Diazinon is rapidly metabolized in mammals and is excreted principally through the urine. It is metabolized in vivo by four enzyme systems, which include mixed function oxidases, hydrolases or phosphatases, glutathione-dependent transferases, and non-specific esterases. Most in vivo animal studies have demonstrated the production of diazoxon, hydroxydiazinon, isohydroxydiazinon, and a propylenediazinon metabolite. Diazinon does not bioaccumulate in tissues or organs.

The mode of action of diazinon, as with other organophosphate insecticides, is inhibition of the enzyme cholinesterase.

### Acute Effects

For technical diazinon, the acute oral LD<sub>50</sub> in rats ranges from 300 to 850 milligrams per kilogram (mg/kg). This rather wide range may be accounted for by the use of various grades of purity of the material and different vehicles of administration. The acute dermal LD<sub>50</sub> for rabbits is 3600 mg/kg and the acute inhalation LC<sub>50</sub> for rats is 3.5 milligrams per liter (mg/l) for 4 hours. For Diazinon 4E, the acute oral LD<sub>50</sub> for rat is 542 mg/kg. The acute dermal LD<sub>50</sub> for rabbit is 600 mg/kg and the acute inhalation LC<sub>50</sub> for rat is 5.4 mg/l for 4 hours. The acute dermal LD<sub>50</sub> of the 25 W formulation was greater than 4,000 mg/kg. Diazinon has not been found either irritating or sensitizing.

One accident involved eight elderly men who drank a solution of diazinon they mistook for wine. Three of them, with an average age of 73 years, died. In another instance, nine men survived the consumption of a beverage they prepared with diazinon emulsion concentrate as one ingredient. These examples and other in which some people have survived the drinking of formulations with only moderate illness and sometimes with little or no treatment, suggest that diazinon is only moderately toxic. A 43 year-old farm worker was brought to the hospital by his wife and his employer because of insomnia the night before and sudden loss of memory during the morning. He was found to have flushing of the abdominal wall, a firm, regular, nontender liver enlarged 2 to 3 cm below the costal margin, and a cholinesterase level only 33% of normal. By next morning he appeared completely recovered. His only known recent exposure to pesticides involved handling diazinon containers a day or two before admission, but there had been no recognized accident and no episode of typical cholinergic illness.

## **Chronic Effects**

Dogs were fed diazinon at 0.25, 0.75, and 75 ppm in the diet for 90 days. Plasma cholinesterase and red-cell cholinesterase were measured. Red-cell cholinesterase was decreased only in the highest-dosage group, and plasma cholinesterase was decreased in the two higher groups. Thus, the no-adverse-effect dosage in this study was 0.25 ppm. Dogs were also used for an 8-month study in which diazinon was administered by gelatin capsule daily at 2.5, 5.0, 10.0, and 20.0 mg/kg. Three of the dogs at the highest dosage died in the first month; one of the dogs at 10.0 mg/kg developed cholinergic symptoms, but recovered. Female rats were fed diets containing diazinon at 1, 5, 25, and 125 ppm for 15-16 weeks. Red-cell cholinesterase was slightly decreased in the 5 ppm group, and no adverse effects were observed at any time in the 1 ppm group. Rats received 10, 100, and 1000 ppm active diazinon as a wettable powder in the diet for 72 weeks with no apparent gross signs of toxicity. Dogs received orally various doses of active diazinon as a wettable powder for 46 weeks. No pathology, gross or microscopic, was observed at the lowest dosage (4.6 mg/kg/day) in 2 weeks. After 12 weeks, cholinesterase inhibition was complete at the lowest dosage. At a dosage of 9.3 mg/kg/day for 5 weeks, signs of toxicity and cholinesterase inhibition were observed. Withdrawal of diazinon at the highest dosage resulted in reversal of signs and regeneration of cholinesterase activity to normal limits after 2 weeks.

## **Mutagenicity**

Diazinon has not been extensively tested for its mutagenic properties. One study on the effect of diazinon on mitosis in human lymphocytes reported chromosomal aberration in 74% of the cells at 0.5 milligrams per milliliter (mg/ml). Diazinon caused significant increase in the frequencies of sister chromatid exchange (SCE) in Umbra limi (central mudminnows).

## **Carcinogenicity**

Diazinon was not carcinogenic to rats and mice. Groups of 50 rats and 50 mice of each sex were administered diazinon at one of two doses, either 400 or 800 ppm for the rats and either 100 or 200 ppm for the mice, for 103 weeks and were then observed for an additional 1 to 2 weeks. Matched controls consisted of groups of 25 untreated rats and 25 untreated mice of each sex. All surviving animals were killed at the end of 104 or 105 weeks. No tumors occurred in any of the dosed groups of rats or mice of either sex.

## **Teratogenicity**

The teratogenic effects of diazinon were investigated in regard to skeletal development, particularly of the extremities and vertebrae. Cartilage and calcified bone were examined in chick embryos of days 5-17 of incubation. Diazinon (200 µg/egg), injected on day 3, inhibited growth of the following skeletal elements: femur, tibia, metatarsi, and digits of the leg. The inhibition was noticeable from the 9<sup>th</sup> day of incubation. The greatest reduction of the skeletal length was observed in tibia and metatarsi, and was characterized by angulations toward the dorsal side.

## **ENVIRONMENTAL EFFECTS**

Diazinon is rapidly degraded in the environment. Several studies have indicated that diazinon is relatively non-persistent in soil. Most diazinon applied is lost from the soil through chemical and biologic degradation within about 2 months of application. There is little information available on the behavior of diazinon in an aquatic environment. It has been reported that about 46% of the diazinon added to neutral aqueous solution remained after 2 weeks. Diazinon does not persist for lengthy periods in either plants or animal tissues.

Diazinon is highly toxic to birds. The acute oral LD<sub>50</sub> (mg/kg) for technical diazinon is: 6.81 for turkey; 40.7 for chicken; 14.7 for goose; 2.75 for gosling. The subacute dietary LC<sub>50</sub> (ppm) for technical diazinon is: 191 for mallard ducks; 245 for bobwhite quail; 244 for ring-necked pheasant; 47 for Japanese quail.

## **STANDARDS AND REGULATIONS**

A Threshold Limit Value (TLV) of 0.1 milligrams per cubic meter (mg/m<sup>3</sup>) and a Short Term Exposure Limit (STEL) value of 0.3 mg/m<sup>3</sup> for diazinon have been established by ACGIH. A large number of tolerances of diazinon in food crops have been established by the Environmental Protection Agency (EPA). These generally range from as low as 0.1 ppm in vegetable crops to as high as 40 ppm in alfalfa as a forage crop. A no-adverse effect level in drinking water has been calculated by the National Academy of Sciences at 0.014 ppm. The acceptable daily intake has been established by WHO/FAO at 0.002 mg/kg/day.

EPA has proposed cancellation of diazinon's use on golf courses and sod farms based on their determination that these uses of the pesticide result in unreasonable adverse effects on birds. The regulatory basis for the EPA action lies in its contention that the use of diazinon on these sites exceeds Special Review risk criteria for acute avian toxicity and chronic effects on avian populations.

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